

AMENDMENT

In the Specification:

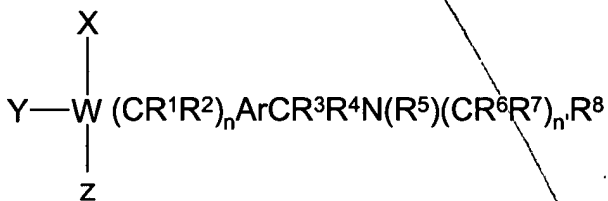
Please replace the paragraph on page 14 lines 3-6 with the following:

D' Further examples of the optionally substituted hydroxyl group include an optionally substituted C₂₋₄alkanoyl (e.g. acetyl, propionyl, butyryl, isobutyryl, etc.), C₁₋₄ alkylsulfonyl (e.g. methanesulfonyl, ethanesulfonyl, etc.) and an optionally substituted aromatic and heterocyclic carboxyl group including benzoyl, pyridinecarboxyl, etc.

In the Claims:

Please replace the presently pending claims with the following claims:

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part
E' 1. (Four times amended) A compound according to Formula I:



(I)

wherein, W is a nitrogen atom and Y is void or, W is a carbon atom and Y=H;

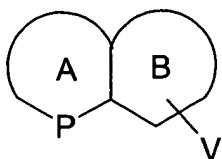
R¹ to R⁷ may be the same or different and are independently hydrogen or straight, branched or cyclic C₁₋₆ alkyl;

R⁸ is an optionally substituted heterocyclic group or an optionally substituted aromatic group

Ar is an aromatic or heteroaromatic ring optionally substituted at single or multiple, non-linking positions with electron-donating or withdrawing groups;

n and n' are independently, 0-2;

X is a group of the formula:



wherein, Ring A is an optionally substituted, saturated or unsaturated 5 or 6-membered ring, and P is an optionally substituted nitrogen atom and wherein any heteroatom in ring A or B is N;

wherein Ring B is an optionally substituted 5 to 7-membered ring;

wherein Ring A or Ring B is bound to group W from any position through group V;

wherein V is a chemical bond or V is a $(CH_2)_n$ group (where $n = 1-2$), or V is a C=O group; and

wherein Z is selected from the group consisting of: a hydrogen atom; an optionally substituted C_{1-6} alkyl group; an optionally substituted aromatic or heterocyclic group; a C_{1-6} alkyl group substituted with an optionally substituted aromatic or heterocyclic group; an optionally substituted amino group; an optionally substituted C_{1-6} alkylamino or C_{3-7} cycloalkylamino group; a sulfonyl group and an optionally substituted carbonyl group; and the pharmaceutically acceptable acid addition salts thereof; and

any stereoisomeric forms and mixtures of stereoisomeric forms thereof.

2. The compound of claim 1, wherein Ring A is selected from the group consisting of: pyridine; pyrimidine; pyrazine; pyridazine; triazine; piperidine; piperazine; imidazole; pyrazole; and triazole and the optionally substituted forms thereof.

3. The compound of claim 1, wherein Ring B is selected from the group consisting of: benzene and a 5 to 7-membered cycloalkyl ring; and the optionally substituted forms thereof.

4. The compound of claim 1, wherein Ring B is selected from the group consisting of: cyclopentyl; cyclohexyl; cycloheptyl; cyclopentenyl; cyclohexenyl; and cycloheptenyl and the optionally substituted forms thereof.

6. The compound of claim 1, wherein Ring A and Ring B together are optionally substituted dihydroquinoline or tetrahydroquinoline.

7. The compound of claim 1, wherein Ring A and Ring B are independently optionally substituted with a substituent selected from the group consisting of: halogen; nitro;

³ cyano; carboxylic acid; an optionally substituted alkyl, alkenyl or cycloalkyl group; an optionally substituted hydroxyl group; an optionally substituted thiol group; an optionally substituted amino or acyl group; an optionally substituted carboxylate, carboxamide or sulfonamide group; and an optionally substituted aromatic or heterocyclic group.

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⁴ 12. The compound of claim 1 wherein said optional substituent in Ring A or Ring B is independently selected from the group consisting of: an optionally substituted aralkyl or heterocycloalkyl, wherein said heterocycloalkyl comprises a 5 or 6 membered ring comprising 1-4 heteroatoms.

13. The compound of claim 12, wherein said optionally substituted aralkyl or heterocycloalkyl is selected from the group consisting of: phenylC₁₋₄alkyl; phenylmethyl (benzyl); phenethyl; pyridinylmethyl; and pyridinylethyl.

⁵ 51. The compound of claim 1, wherein Z is an optionally substituted C₁₋₆alkyl group, wherein said C₁₋₆alkyl group is substituted with one or more substituents selected from the group consisting of: halogen; nitro; cyano; carboxylic acid; an optionally substituted alkyl, alkenyl or cycloalkyl group; an optionally substituted hydroxyl group; an optionally substituted thiol group; an optionally substituted amino or acyl group; an optionally substituted carboxylate, carboxamide or sulfonamide group; and an optionally substituted aromatic or heterocyclic group.

⁶ 55. (Amended) The compound of claim 1, wherein Z is an optionally substituted aromatic or heterocyclic group or a C₁₋₆alkyl group optionally substituted with an optionally substituted aromatic or heterocyclic group.

³ 56. The compound of claim 55, wherein said optionally substituted aromatic group is substituted with a substituent selected from the group consisting of: benzene; naphthalene; dihydronaphthalene; and tetrahydronaphthalene; and wherein said optionally substituted heterocyclic group is selected from the group consisting of: a 5 to 6-membered saturated, partially saturated, or aromatic heterocyclic ring comprising 1 to 4 heteroatoms selected from nitrogen, oxygen and sulfur.

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57. The compound of claim 56, wherein said heterocyclic group is selected from the group consisting of: pyridine, quinoline, isoquinoline, imidazole, benzimidazole, azabenzimidazole, benzotriazole, furan, benzofuran, thiazole, benzothiazole, oxazole, benzoxazole, pyrrole, indole, indoline, indazole, pyrrolidine, pyrrolidone, pyrroline, piperidine, piperazine, tetrahydroquinoline, tetrahydroisoquinoline, pyrazole, thiophene, isoxazole, isothiazole, triazole, tetrazole, oxadiazole, thiadiazole, morpholine, thiamorpholine, pyrazolidine, imidazolidine, imidazoline, tetrahydropyran, dihydropyran, benzopyran, dioxane, dithiane, tetrahydrofuran, tetrahydrothiophene, dihydrofuran, and dihydrothiophene.

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58. The compound of claim 57, wherein said heterocyclic group comprises nitrogen or sulfur heteroatoms; and wherein said nitrogen or sulfur heteroatoms may optionally be in the form of oxides.

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98. A compound of claim 1 selected from the group consisting of:
- (a) AMD8862, N-(2-pyridinylmethyl)-N'-[2-[(1H-imidazol-4-ylmethyl)amino]ethyl]-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzene dimethanamine;
 - (b) AMD8887, N-(2-pyridinylmethyl)-N'-[2-[(1H-imidazol-2-ylmethyl)amino]ethyl]-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
 - (c) AMD8816, N-(2-pyridinylmethyl)-N'-[2-(phenylureido)ethyl]-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
 - (d) AMD8737, N-(2-pyridinylmethyl)-N'-[[N'-(n-butyl)carboxamido]methyl]-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
 - (e) AMD8739, N-(2-pyridinylmethyl)-N'-(carboxamidomethyl)-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
 - (f) AMD8752, N-(2-pyridinylmethyl)-N'-[(N'-phenyl)carboxamidomethyl]-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
 - (g) AMD8765, N-(2-pyridinylmethyl)-N'-(carboxymethyl)-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
 - (h) AMD8715, N-(2-pyridinylmethyl)-N'-(phenylmethyl)-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
 - (i) AMD8907, N-(2-pyridinylmethyl)-N'-(1H-benzimidazol-2-ylmethyl)-N'-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;

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- (j) AMD8927, N-(2-pyridinylmethyl)-N'-(5,6-dimethyl-1*H*-benzimidazol-2-ylmethyl)-N'-(5,6,7,8-tetrahydro-8-quinolinyl)-1,4-benzenedimethanamine (hydrobromide salt);
 - (k) AMD8926, N-(2-pyridinylmethyl)-N'-(5-nitro-1*H*-benzimidazol-2-ylmethyl)-N'-(5,6,7,8-tetrahydro-8-quinolinyl)-1,4-benzenedimethanamine;
 - (l) AMD8929, N-(2-pyridinylmethyl)-N'-[(1*H*)-5-azabenzimidazol-2-ylmethyl]-N'-(5,6,7,8-tetrahydro-8-quinolinyl)-1,4-benzenedimethanamine;
 - (m) AMD8931, N-(2-pyridinylmethyl)-N-(4-phenyl-1*H*-imidazol-2-ylmethyl)-N'-(5,6,7,8-tetrahydro-8-quinolinyl)-1,4-benzenedimethanamine;
 - (n) AMD8783, N-(2-pyridinylmethyl)-N'-[2-(2-pyridinyl)ethyl]-N'-(5,6,7,8-tetrahydro-8-quinolinyl)-1,4-benzenedimethanamine;
 - (o) AMD8764, N-(2-pyridinylmethyl)-N'-(2-benzoxazolyl)-N'-(5,6,7,8-tetrahydro-8-quinolinyl)-1,4-benzenedimethanamine;
 - (p) AMD8780, N-(2-pyridinylmethyl)-N'-(*trans*-2-aminocyclohexyl)-N'-(5,6,7,8-tetrahydro-8-quinolinyl)-1,4-benzenedimethanamine;
 - (q) AMD8818, N-(2-pyridinylmethyl)-N'-(2-phenylethyl)-N'-(5,6,7,8-tetrahydro-8-quinolinyl)-1,4-benzenedimethanamine;
 - (r) AMD8829, N-(2-pyridinylmethyl)-N'-(3-phenylpropyl)-N'-(5,6,7,8-tetrahydro-8-quinolinyl)-1,4-benzenedimethanamine;
 - (s) AMD8839, N-(2-pyridinylmethyl)-N'-(*trans*-2-aminocyclopentyl)-N'-(5,6,7,8-tetrahydro-8-quinolinyl)-1,4-benzenedimethanamine;
 - (t) AMD8726, N-[[4-[(2-pyridinylmethyl)amino]methyl]phenyl]methyl]-N-(5,6,7,8-tetrahydro-8-quinolinyl)-glycinamide;
 - (u) AMD8738, N-[[4-[(2-pyridinylmethyl)amino]methyl]phenyl]methyl]-N-(5,6,7,8-tetrahydro-8-quinolinyl)-(L)-alaninamide;
 - (v) AMD8749, N-[[4-[(2-pyridinylmethyl)amino]methyl]phenyl]methyl]-N-(5,6,7,8-tetrahydro-8-quinolinyl)-(L)-aspartamide;
 - (w) AMD8750, N-[[4-[(2-pyridinylmethyl)amino]methyl]phenyl]methyl]-N-(5,6,7,8-tetrahydro-8-quinolinyl)-pyrazinamide;
 - (x) AMD8740, N-[[4-[(2-pyridinylmethyl)amino]methyl]phenyl]methyl]-N-(5,6,7,8-tetrahydro-8-quinolinyl)-(L)-prolinamide;
 - (y) AMD8741, N-[[4-[(2-pyridinylmethyl)amino]methyl]phenyl]methyl]-N-(5,6,7,8-tetrahydro-8-quinolinyl)-(L)-lysineamide;

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- (z) AMD8724, N-[[4-[(2-pyridinylmethyl)amino]methyl]phenyl]methyl]-N-(5,6,7,8-tetrahydro-8-quinolinyl)-benzamide;
- (aa) AMD8725, N-[[4-[(2-pyridinylmethyl)amino]methyl]phenyl]methyl]-N-(5,6,7,8-tetrahydro-8-quinolinyl)-picolinamide;
- (bb) AMD8713, N'-Benzyl-N-[[4-[(2-pyridinylmethyl) amino]methyl]phenyl]methyl]-N-(5,6,7,8-tetrahydro-8-quinolinyl)-urea;
- (cc) AMD8712, N'-phenyl-N-[[4-[(2-pyridinylmethyl) amino]methyl]phenyl]methyl]-N-(5,6,7,8-tetrahydro-8-quinolinyl)-urea;
- (dd) AMD8716, N-(6,7,8,9-tetrahydro-5H-cyclohepta[bacteriapyridin-9-yl]-4-[(2-pyridinylmethyl)amino]methyl]benzamide;
- (ee) AMD8717, N-(5,6,7,8-tetrahydro-8-quinolinyl)-4-[(2-pyridinylmethyl)amino]methyl]benzamide;
- (ff) AMD8634, N,N'-bis(2-pyridinylmethyl)-N'-(5,6,7,8-tetrahydro-8-quinolinyl)-1,4-benzenedimethanamine;
- (gg) AMD8774, N,N'-bis(2-pyridinylmethyl)-N'-(6,7,8,9-tetrahydro-5H-cyclohepta[bacteriapyridin-9-yl]-1,4-benzenedimethanamine;
- (hh) AMD8775, N,N'-bis(2-pyridinylmethyl)-N'-(6,7-dihydro-5H-cyclopenta[bacteriapyridin-7-yl]-1,4-benzenedimethanamine;
- (ii) AMD8819, N,N'-bis(2-pyridinylmethyl)-N'-(1,2,3,4-tetrahydro-1-naphthalenyl)-1,4-benzenedimethanamine;
- (jj) AMD8768, N,N'-bis(2-pyridinylmethyl)-N'-[(5,6,7,8-tetrahydro-8-quinolinyl)methyl]-1,4-benzenedimethanamine;
- (kk) AMD8767, N,N'-bis(2-pyridinylmethyl)-N'-[(6,7-dihydro-5H-cyclopenta[bacteriapyridin-7-yl)methyl]-1,4-benzenedimethanamine;
- (ll) AMD8838, N-(2-pyridinylmethyl)-N-(2-methoxyethyl)-N'-(5,6,7,8-tetrahydro-8-quinolinyl)-1,4-benzenedimethanamine;
- (mm) AMD8871, N-(2-pyridinylmethyl)-N-[2-(4-methoxyphenyl)ethyl]-N'-(5,6,7,8-tetrahydro-8-quinolinyl)-1,4-benzenedimethanamine;
- (nn) AMD8844, N,N'-bis(2-pyridinylmethyl)-1,4-(5,6,7,8-tetrahydro-8-quinolinyl)benzenedimethanamine;
- (oo) AMD7129, N-[(2,3-dimethoxyphenyl)methyl]-N'-(2-pyridinylmethyl)-N-(5,6,7,8-tetrahydro-8-quinolinyl)-1,4-benzenedimethanamine;

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- (pp) AMD7130, N,N'-bis(2-pyridinylmethyl)-N-[1-(N''-phenyl-N''-methylureido)-4-piperidinyl]-1,3-benzenedimethanamine;
- (qq) AMD7131, N,N'-bis(2-pyridinylmethyl)-N-[N''-p-toluenesulfonylphenylalanyl]-4-piperidinyl]-1,3-benzenedimethanamine;
- (rr) AMD7136, N,N'-bis(2-pyridinylmethyl)-N-[1-[3-(2-chlorophenyl)-5-methyl-isoxazol-4-oyl]-4-piperidinyl]-1,3-benzenedimethanamine;
- (ss) AMD7138, N-[(2-hydroxyphenyl)methyl]-N'-(2-pyridinylmethyl)-N-(6,7,8,9-tetrahydro-5H-cyclohepta[bacteriapyridin-9-yl])-1,4-benzenedimethanamine;
- (tt) AMD7140, N-[(4-cyanophenyl)methyl]-N'-(2-pyridinylmethyl)-N-(6,7,8,9-tetrahydro-5H-cyclohepta[bacteriapyridin-9-yl])-1,4-benzenedimethanamine;
- (uu) AMD7141, N-[(4-cyanophenyl)methyl]-N'-(2-pyridinylmethyl)-N-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
- (vv) AMD7142, N-[(4-acetamidophenyl)methyl]-N'-(2-pyridinylmethyl)-N-(5,6,7,8-tetrahydro-8-quinoliny)-1,4-benzenedimethanamine;
- (ww) AMD7145, N-[(4-phenoxyphenyl)methyl]-N'-(2-pyridinylmethyl)-N-(6,7,8,9-tetrahydro-5H-cyclohepta[bacteriapyridin-9-yl])-1,4-benzenedimethanamine;
- (xx) AMD7147, N-[(1-methyl-2-carboxamido)ethyl]-N,N'-bis(2-pyridinylmethyl)-1,3-benzenedimethanamine;
- (yy) AMD7151, N-[(4-benzyloxyphenyl)methyl]-N'-(2-pyridinylmethyl)-N-(6,7,8,9-tetrahydro-5H-cyclohepta[bacteriapyridin-9-yl])-1,4-benzenedimethanamine; and
- (zz) AMD7155, N-[(thiophene-2-yl)methyl]-N'-(2-pyridinylmethyl)-N-(6,7,8,9-tetrahydro-5H-cyclohepta[bacteriapyridin-9-yl])-1,4-benzenedimethanamine.

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102. (Twice amended) A pharmaceutical composition comprising a therapeutically effective amount of the compound of claim 1 in admixture with at least one pharmaceutically acceptable excipient.

Please add the following claims:

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119. (New) The compound of claim 1, wherein W is a nitrogen atom.

120. (New) The compound of claim 119, wherein Ring A is selected from the group consisting of: pyridine; pyrimidine; pyrazine; pyridazine; triazine; piperidine; piperazine; imidazole; pyrazole; and triazole and the optionally substituted forms thereof.

121. (New) The compound of claim 119, wherein Ring B is selected from the group consisting of: benzene and a 5 to 7-membered cycloalkyl ring; and the optionally substituted forms thereof.

122. (New) The compound of claim 119, wherein Ring B is selected from the group consisting of: cyclopentyl; cyclohexyl; cycloheptyl; cyclopentenyl; cyclohexenyl; and cycloheptenyl and the optionally substituted forms thereof.

123. (New) The compound of claim 119, wherein Ring A and Ring B together are optionally substituted dihydroquinoline or tetrahydroquinoline.

124. (New) The compound of claim 119, wherein Ring A and Ring B are independently optionally substituted with a substituent selected from the group consisting of: halogen; nitro; cyano; carboxylic acid; an optionally substituted alkyl, alkenyl or cycloalkyl group; an optionally substituted hydroxyl group; an optionally substituted thiol group; an optionally substituted amino or acyl group; an optionally substituted carboxylate, carboxamide or sulfonamide group; and an optionally substituted aromatic or heterocyclic group.

125. (New) The compound of claim 119 wherein said optional substituent in Ring A or Ring B is independently selected from the group consisting of: an optionally substituted aralkyl or heterocycloalkyl, wherein said heterocycloalkyl comprises a 5 or 6 membered ring comprising 1-4 heteroatoms.

126. (New) The compound of claim 125, wherein said optionally substituted aralkyl or heterocycloalkyl is selected from the group consisting of: phenylC₁₋₄alkyl; phenylmethyl (benzyl); phenethyl; pyridinylmethyl; and pyridinylethyl.

127. (New) The compound of claim 119, wherein Z is an optionally substituted C₁₋₆alkyl group, wherein said C₁₋₆alkyl group is substituted with one or more substituents selected from the group consisting of: halogen; nitro; cyano; carboxylic acid; an optionally substituted alkyl, alkenyl or cycloalkyl group; an optionally substituted hydroxyl group; an optionally substituted thiol group; an optionally substituted amino or acyl group; an optionally substituted carboxylate, carboxamide or sulfonamide group; and an optionally substituted aromatic or heterocyclic group.

128. (New) The compound of claim 119, wherein Z is an optionally substituted aromatic or heterocyclic group or a C₁₋₆alkyl group optionally substituted with an optionally substituted aromatic or heterocyclic group.

129. (New) The compound of claim 128, wherein said optionally substituted aromatic group is substituted with a substituent selected from the group consisting of: benzene; naphthalene; dihydronaphthalene; and tetrahydronaphthalene; and wherein said optionally substituted heterocyclic group is selected from the group consisting of: a 5 to 6-membered saturated, partially saturated, or aromatic heterocyclic ring comprising 1 to 4 heteroatoms selected from nitrogen, oxygen and sulfur.

130. (New) The compound of claim 129, wherein said heterocyclic group is selected from the group consisting of: pyridine, quinoline, isoquinoline, imidazole, benzimidazole, azabenzimidazole, benzotriazole, furan, benzofuran, thiazole, benzothiazole, oxazole, benzoxazole, pyrrole, indole, indoline, indazole, pyrrolidine, pyrrolidone, pyrroline, piperidine, piperazine, tetrahydroquinoline, tetrahydroisoquinoline, pyrazole, thiophene, isoxazole, isothiazole, triazole, tetrazole, oxadiazole, thiadiazole, morpholine, thiamorpholine, pyrazolidine, imidazolidine, imidazoline, tetrahydropyran, dihydropyran, benzopyran, dioxane, dithiane, tetrahydrofuran, tetrahydrothiophene, dihydrofuran, and dihydrothiophene.

131. (New) The compound of claim 130, wherein said heterocyclic group comprises nitrogen or sulfur heteroatoms; and wherein said nitrogen or sulfur heteroatoms may optionally be in the form of oxides.

09 132. (New) A pharmaceutical composition comprising a therapeutically effective amount of the compound of claim 119 in admixture with at least one pharmaceutically acceptable excipient.

Please replace the Abstract with the following:

Compounds containing heterocycles linked through an aromatic group are disclosed as useful in modulating chemokine mediated reactions.